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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/800,266	03/05/2001	Robert L. Bratzler	C1037/7017 (HCL/MAT)	3753

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EXAMINER

ANGELL, JON E

ART UNIT PAPER NUMBER

1635

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/800,266

Applicant(s)

BRATZLER ET AL.

Examiner

J. Eric Angell

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 06 March 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-17 and 31 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-17 and 31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### DETAILED ACTION

1. This Action is in response to the communication filed on 3/6/03, as Paper No. 11. The amendment has been entered. Claims 21 and 36 have been cancelled. Claims 1-17 and 31 are currently pending in the application and are addressed herein.
2. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-17 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for inhibiting tumor cell growth in a subject having cancer, wherein said method comprises administering to said subject:

- a) a poly-G nucleic acid; and
- b) a cancer medicament;

wherein the poly-G nucleic acid is not conjugated to the cancer medicament, and wherein the administration of said poly-G nucleic acid and said cancer medicament results in the inhibition of tumor cell growth in said subject.

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Does not reasonably provide enablement for the full scope encompassed by the claims.

Specifically, the specification is not enabling for a method of preventing/curing cancer in a subject.

Furthermore, the claims encompass administering a cancer medicament that is a cancer vaccine (see, e.g., claims 2 and 4). While the specification enables the claims to the extent that the claims read on a method for inhibiting tumor cell growth in a subject having cancer by administering a poly-G nucleic acid and a cancer medicament that is a therapeutic compound, the specification does not enable the claims for said method comprising administering a poly-G nucleic acid and a cancer vaccine because the art does not recognize that there are any known cancer vaccines which can cure cancer or prevent the occurrence of any future cancer in a subject for the reasons set forth below.

Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

*Wands* states on page 1404,

“Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”

The nature of the invention

The instant claims are drawn to methods of treating and preventing or curing of cancer using a poly-G nucleic acid in combination with a cancer medicament.

The breadth of the claims

The claims are very broad. The broadest claims (e.g. claim 1) encompass treating or preventing any type of cancer by administering to a subject any poly-G nucleic acid and any cancer medicament.

The unpredictability of the art and the state of the prior art

As mentioned above, the specification does not enable the claims for prevention or curing of cancer. At the time of filing there were no methods known in the art for using immunostimulatory oligonucleotides in combination with a cancer medicament for the prevention/curing of cancer. As mentioned in the previous Office Action, the prior and post filing art does indicate that there a number of problems related to cancer immunotherapy in general and which do apply to the instant claimed method as they read on preventing/curing cancer.

It is respectfully pointed out that the claimed invention encompasses the administration of an immunostimulatory oligonucleotide to boost the subject's immune response. Administration of the cancer medicament is intended to lyse the cancer cells, resulting in the release of cancer specific antigens. The immune response (which is enhanced due to the immunostimulatory nucleotide sequence) would then be directed against the cancer antigen, and theoretically against cancer cells expressing the cancer antigen (see Applicants response filed 3/6/03, p. 4-5). Therefore, the claimed invention encompasses immunotherapy for the prevention/curing of

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cancer as well as treating cancer. Applicants' arguments and submitted material are sufficient to indicate that the claims are enabled for treating (i.e. inhibiting) tumor cell growth, but not for curing or preventing any future occurrence of cancer, because the relevant art indicates that there were no known methods for curing cancer or for preventing the future occurrence of cancer. The art cited in the previous Office Action is relevant to the broad claims presently pending because they point out some of the problems associated with cancer immunotherapy for curing/preventing cancer.

The relevant art teaches that immunotherapy of cancer with regards to preventing/curing cancer is unpredictable. For instance, Gouttefangeas et al. (Nature Biotechnology Vol. 18:491-492; 2000) teaches, "effective immunotherapy has remained elusive because of three major problems: first, for many tumors, no or not enough suitable antigens are known; second, no consensus exists for the best antigen formulations or the route of immunization; and third, tumors under immune attack tend to be selected for antigen loss variants." (See p. 491, first paragraph). Specifically regarding the immunostimulatory effects of oligodeoxynucleotides, Gouttefangeas points out, "[W]e do not yet know whether such constructs [immunostimulatory oligonucleotides] work in humans. Some immunostimulatory effects of CpG motifs have been described in human peripheral blood in vitro, most notably in dendritic cells, but immunization trials have not been reported. Thus, the efficacy of CpG-protein constructs for immunotherapy in patients remains to be tested." (See p. 492, middle column, first paragraph). Therefore, Gouttefangeas teaches that there has been no identification of any cancer immunizing oligonucleotides in humans. Thus no "master drug" has been identified for curing or preventing cancer.

Furthermore, Old (1996), as previously mentioned, teaches that there are several problems associated with cancer immunotherapy. For instance, Old teaches, "Despite the great hope of immunotherapy, a dark cloud hangs over all our attempts to control cancer by immune mechanisms. Cancer cells are masters of deceit and disguise-veritable Houdinis that can readily alter themselves to evade immunological recognition and attack." (See p. 11, under "The hurdles ahead"). Furthermore, Old teaches, "[I]t is conceivable that cancer vaccines may injure normal cells to some degree" and points out, "There are a number of disease states, called autoimmune diseases, that arise when the immune system turns against normal tissues in the body." (See p. 11, under "The hurdles ahead"). Finally, Old teaches, "[W]e need to exert considerable caution in making any predictions" clearly indicating the unpredictable nature of immunotherapy (See p. 11, under "The hurdles ahead").

Although the methods reviewed by Old encompass immunotherapy in general (and very broadly) the problems indicated by Old are relevant to the presently claimed invention because the basic mechanism—immune response directed to cancer cells displaying cancer-specific antigens—are the same, even if the claimed method steps are not identical.

Furthermore, it is respectfully pointed out that the claims encompass preventing/curing cancer in a subject. Preventing cancer using the instant method encompasses administering the therapeutic compounds to individuals who do not have cancer, and would encompass administering the immunostimulatory nucleic acid and the cancer medicament (such as a chemotherapeutic drug) to normal (i.e. cancer-free) individuals. Considering the teachings of the prior art that cancer vaccines may injure normal cells and induce autoimmune disease, and also

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considering that the instant invention encompasses administering an immunostimulatory agent and agent intended to lyse cells (i.e. the cancer medicament), it is clear that there are a number of obstacles that must be overcome before the claimed invention could be used to prevent cancer in a subject.

Additionally, there is no indication in the prior art or in the post filing art that there is any method which can be used to cure or prevent the future occurrence of cancer in a subject.

Regarding the use of a "cancer vaccine" in the method for curing/preventing cancer, it is respectfully pointed out that the relevant art at the time of filing indicates that there were no known cancer vaccines which could cure or prevent any future occurrence of cancer in a subject.

For instance, Bodey et al. (Anticancer Research Vol. 20:2665-2676; 2000) teaches,

"Although general immune activation directed against the target antigens contained within the cancer vaccine has been documented in most cases, reduction in tumor load has not been frequently observed, and tumor progression and metastasis usually ensue, possibly following a slightly extended period of remission. The failure of cancer vaccine to fulfill their promise is due to the very relationship between host and tumor: through a natural selection process the host leads to the selective enrichment of clones and highly aggressive neoplastic transformed cells..."; "The use of cancer vaccines seems, at present, destined to remain limited to their employment as adjuvants to both traditional therapies and in the management of minimal residual disease following surgical resection or the primary cancer mass." (See p. 2665, abstract, second column); and,

"[T]he cancer vaccine approach to immunotherapy has been shown in most cases to result in an in vitro or s.c.... enhancement of TAA targeted immunity. However, even after considerable remission (which has not been shown to be strictly induced by vaccination), the malignant tumor does in most cases progress and overwhelm the host. This apparent contradiction is the defining characteristic of the difficulties associated with an immunological approach to cancer therapy, including the generation of cancer vaccines." (See p. 2673, first column).

Therefore, Bodey clearly indicates that recurrence of cancer after initial successful treatment of a tumor with an immunotherapeutic composition is common, indicating that cancer vaccines cannot predictably cure or prevent the future occurrence of cancer in a subject.



Working Examples and Guidance in the Specification

As mentioned in the previous Office Action, the specification does not disclose any working examples which clearly indicate that the method can be used to prevent cancer in a subject.

It is acknowledged that the specification discloses guidance on the administration of the therapeutic compounds to a subject, thus indicating how to administer the compounds, but there is no disclosure indicating that the method could prevent the occurrence of any future cancer.

Quantity of Experimentation

As mentioned above, there are a number of problems related to immunotherapy which apply to the claimed method, including autoimmune disorders, as well as the ability of cancer cells to adapt and evade the immune response. Furthermore, the claims encompass the prevention of cancer and the relevant art does not teach any methods which can be used to prevent cancer in a subject. Therefore, in order to practice the claimed invention to prevent cancer in a subject one of skill in the art would have to perform additional experimentation. The additional experimentation would require the testing of the method in cancer-free individuals to test for the possibility that the method could result in autoimmune disease. Furthermore, the experimentation would have to indicate that the method could be used to prevent any future occurrence of any type of cancer in the subject. This would require years of experimentation in order to show that the treatment could prevent any future occurrence of cancer.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the of unpredictable nature of cancer prevention, the breadth of the claims, the lack of any working examples in the specification; and the high degree of skill required, it is concluded that the amount of experimentation required to perform the broadly claimed method for preventing cancer is undue.

***Response to Arguments***

5. Applicant's arguments, see pages 2-8, filed 3/6/03, with respect to the rejection(s) of claims under 35 USC 112, first paragraph have been fully considered and are not fully persuasive. Specifically, Applicants' arguments are persuasive only to the extent that the claims are drawn to a method for inhibiting tumor cell growth in a subject having cancer. However, there is no data presented which overcomes the unpredictable nature associated with curing or preventing cancer in an individual. Regarding Applicants' argument that the cited prior art references do not apply to the presently claimed invention, it is respectfully pointed out that the methods described in the prior art references are very similar (but not identical) to the claimed invention, and are applicable because they teach problems associated with immunotherapy and cancer vaccination in general. Furthermore, the references are being used to indicate that the claims are not enabled for curing or preventing cancer in a subject, not inhibiting cancer cell growth. Regarding Applicants arguments that the Old reference is not an indication of the state of the art at the time of filing, it is respectfully pointed out that the reference indicates a number of problems associated with cancer immunotherapy. Regardless of the date of publication, Applicants have not submitted data or references which overcome the problems indicated by Old with respect to curing or preventing cancer. Therefore, absent evidence to the contrary Old does appropriately indicate the state of the art at the time of filing.

In summary, Applicants arguments are persuasive only to the extent that the method can be used to inhibit tumor cell growth in a subject having cancer using a poly-G nucleic acid and a cancer medicament (wherein the medicament is a therapeutic compound). However, the claims are very broad and encompass curing and preventing cancer in a subject using a nucleic acid sequence and a "cancer vaccine". For the reasons stated above, the claims are not enabled in commensurate scope with the claims. Amending the claims such that they do not read on preventing/curing cancer (such as indicated above) would obviate this rejection.

***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 10 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 10 recites the limitation "the immunostimulatory nucleic acid" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 11 depends on claim 10 and is therefore also rejected for the same reason.

***Claim Rejections - 35 USC § 102***

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1, 2 and 10-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Bennett et al. (US Patent 6,172,216 B1).

The instant claims are drawn to (in general) a method for treating cancer in a subject by administering a poly-G nucleic acid and a cancer medicament.

Bennett clearly teaches a method of treating cancer in a subject by administering to the subject an oligonucleotide sequence comprising the sequence CTGGGCC (see SEQ ID NO: 10, Table 1, column 27). It is pointed out that the specification indicates that the immunostimulatory poly-G nucleic acid preferably comprises the sequence XXGGGXX (see p. 12, lines 20-30 of the specification). Therefore, the oligonucleotide meets all of the structural limitations set forth in the specification to be an immunostimulatory poly-G nucleic acid. Furthermore, Bennett also teaches that the oligonucleotide can be combined with a cancer chemotherapeutic compound (not conjugated) to form a pharmaceutical composition (e.g., see claims 1, 11 and 34). Bennett indicates that the oligonucleotide/chemotherapeutic composition can be used to treat cancer (e.g., see Col. 1, lines 1-10; Col. 1, line 65 through Col. 2, line 21; and Col. 15, lines 12-65). Bennett also teaches that the oligonucleotide can comprise a modified backbone, including a phosphorothioate-modified backbone (e.g., see Col. 6, line 55 through Col. 7, line 10). It is also pointed out that the Bennett's oligonucleotide that is SEQ ID NO: 10, is free of any CpG motifs and poly-T motifs.

11. Claim 31 is rejected under 35 U.S.C. 102(e) as being anticipated by Krieg (US Patent 6,218,371).

The instant claim is drawn to a method for treating cancer by administering to a subject an immunostimulatory nucleic acid (CpG or non-CpG) and a cancer medicament that is a hormone therapy.

Krieg teaches a method for treating cancer in a subject wherein the treatment comprises administering to a subject a composition comprising a combination of an immunostimulatory CpG nucleic acid and a hormone therapy (e.g., see Col. 3, lines 5-53; Col. 27, lines 24-36). Therefore, Krieg anticipates claim 31.

***Claim Rejections - 35 USC § 103***

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1, 3, 6-9, 12, 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett (US 6,172,216) in view of Muller (WO 97/32604).

Claims 1 and 12 are rejected by Bennett's teaching of a method for treating cancer in a subject by administering to the subject an oligonucleotide sequence comprising the sequence CTGGGCC (see SEQ ID NO: 10, Table 1, column 27). It is pointed out that the specification indicates that the immunostimulatory poly-G nucleic acid preferably comprises the sequence XXGGGXX (see p. 12, lines 20-30 of the specification). Therefore, the oligonucleotide meets all of the structural limitations set forth in the specification to be an immunostimulatory poly-G nucleic acid. Furthermore, Bennett also teaches that the oligonucleotide can be combined with a cancer chemotherapeutic compound (not conjugated) to form a pharmaceutical composition (e.g., see claims 1, 11 and 34). Bennett indicates that the oligonucleotide/chemotherapeutic composition can be used to treat cancer (e.g., see Col. 1, lines 1-10; Col. 1, line 65 through Col. 2, line 21; and Col. 15, lines 12-65). Bennett also teaches that the oligonucleotide can comprise a modified backbone, including a phosphorothioate-modified backbone (e.g., see Col. 6, line 55 through Col. 7, line 10). It is also pointed out that the Bennett's oligonucleotide that is SEQ ID NO: 10, is free of any CpG motifs and poly-T motifs.

Bennett does not teach that 1) the chemotherapeutic agent is Taxol/Paclitaxel (claims 3, 7, 15); 2) the cancer medicament is a hormone therapy (claim 6); 3) the method further comprises administering IFN-alpha to the subject (claims 8, 16); and 4) the cancer is skin cancer (claim 9).

However, Muller teaches a method of treating cancer using a combination therapy comprising administering to a subject a composition comprising an oligonucleotide sequence

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(not a poly-G oligonucleotide) in combination with a chemotherapeutic agent, such as taxol, a hormonal agent, and interferon-alpha (IFN-alpha) (e.g., see p. 1, first full paragraph; p. 32, lines 10-15; p. 33, under p(E); and p. 34, under (F) and (I)). Furthermore, Muller indicates that the combination therapy could be used to treat a variety of cancers, such as melanoma (a form of skin cancer) (e.g., see p. 26, lines 1-5).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to make the claimed invention using the teachings of Bennett and Muller with a reasonable expectation of success. In order to make the claimed invention one of skill in the art could combine the references such that the method of Bennett is modified so that the therapeutic composition that is administered to the subject comprises the poly-G nucleic acid taught by Bennett in combination with taxol, a hormonal agent, and further comprises IFN-alpha for the treatment of a skin cancer, as taught by Muller.

One of ordinary skill would have been motivated to make the modifications to the therapeutic composition because Muller indicates that taxol, hormonal agents, and IFN-alpha are effective cancer therapeutic compounds which can be used in combination with other therapeutic compounds for treating proliferative diseases such as melanoma.

15. Claims 1, 2 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett (US 6,172,216) in view of Dannenberg (US Patent 6,403,630).

Claims 1 and 2 are rejected by Bennett's teaching of a method for treating cancer in a subject by administering to the subject an oligonucleotide sequence comprising the sequence CTGGGCC (see SEQ ID NO: 10, Table 1, column 27). It is pointed out that the specification

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indicates that the immunostimulatory poly-G nucleic acid preferably comprises the sequence XXGGGXX (see p. 12, lines 20-30 of the specification). Therefore, the oligonucleotide meets all of the structural limitations set forth in the specification to be an immunostimulatory poly-G nucleic acid. Furthermore, Bennett also teaches that the oligonucleotide can be combined with a cancer therapeutic compound (not conjugated) to form a pharmaceutical composition (e.g., see claims 1, 11 and 34). Bennett indicates that the oligonucleotide/cancer therapeutic composition can be used to treat cancer (e.g., see Col. 1, lines 1-10; Col. 1, line 65 through Col. 2, line 21; and Col. 15, lines 12-65). Bennett also teaches that the oligonucleotide can comprise a modified backbone, including a phosphorothioate-modified backbone (e.g., see Col. 6, line 55 through Col. 7, line 10). It is also pointed out that the Bennett's oligonucleotide that is SEQ ID NO: 10, is free of any CpG motifs and poly-T motifs.

Bennett does not teach that the cancer therapeutic agent is Herceptin (claim 4).

However, Dannenberg teaches a method for treating cancer comprising administering to a subject having cancer a composition comprising the combination of two anti-cancer agents, one of which is Herceptin (e.g., see abstract; Col. 1, lines 19-36; Col. 2, lines 4-15; Col. 11, lines 15-45; and claim 1).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to make the claimed invention using the teachings of Bennett and Dannenberg with a reasonable expectation of success. In order to make the claimed invention one of skill in the art could combine the references such that the method of Bennett is modified so that the therapeutic composition that is administered to the subject comprises the poly-G nucleic acid taught by Bennett in combination with Herceptin as taught by Dannenberg.



One of ordinary skill would have been motivated to make the modifications to the therapeutic composition because Dannenberg indicates that Herceptin is an effective anti-cancer cancer agent which can be used in combination with other therapeutic compounds for treating cancer.

16. Claims 1, 2, 5, 12 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett (US 6,172,216) in view of Eberlein (US Patent 5,550,214).

As indicated in the 112, first paragraph rejection above, the claims encompass administering a cancer vaccine, which is not fully enabled. The instant claims are however, enabled to the extent that the claims read on administering an anti-cancer agent (i.e., a cancer therapeutic agent) such as Her2/neu, a cancer specific antigen. The instant claims are interpreted as encompassing administering a combination comprising a cancer specific antigen, such as Her2/neu.

Claims 1, 2 and 12 are rejected by Bennett's teaching of a method for treating cancer in a subject by administering to the subject an oligonucleotide sequence comprising the sequence CTGGGCC (see SEQ ID NO: 10, Table 1, column 27). It is pointed out that the specification indicates that the immunostimulatory poly-G nucleic acid preferably comprises the sequence XXGGGXX (see p. 12, lines 20-30 of the specification). Therefore, the oligonucleotide meets all of the structural limitations set forth in the specification to be an immunostimulatory poly-G nucleic acid. Furthermore, Bennett also teaches that the oligonucleotide can be combined with a cancer therapeutic compound (not conjugated) to form a pharmaceutical composition (e.g., see claims 1, 11 and 34). Bennett indicates that the oligonucleotide/cancer therapeutic composition

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can be used to treat cancer (e.g., see Col. 1, lines 1-10; Col. 1, line 65 through Col. 2, line 21; and Col. 15, lines 12-65). Bennett also teaches that the oligonucleotide can comprise a modified backbone, including a phosphorothioate-modified backbone (e.g., see Col. 6, line 55 through Col. 7, line 10). It is also pointed out that the Bennett's oligonucleotide that is SEQ ID NO: 10, is free of any CpG motifs and poly-T motifs.

Bennett does not teach that the cancer therapeutic agent is a cancer antigen, such as a Her2/neu peptide (claims 5 and 17).

However, Eberlein teaches a method for treating cancer comprising administering to a subject having cancer a composition comprising the cancer antigen that is a Her2/neu peptide (e.g., see abstract, Col. 2, lines 25-50; Col. 17, lines 58-67).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to make the claimed invention using the teachings of Bennett and Eberlein with a reasonable expectation of success. In order to make the claimed invention one of skill in the art could combine the references such that the method of Bennett is modified so that the therapeutic composition that is administered to the subject comprises the poly-G nucleic acid taught by Bennett in combination with the cancer antigen Her2/Neu peptide taught by Eberlein.

One of ordinary skill would have been motivated to make the modifications to the therapeutic composition because Eberlein indicates that the Her2/neu peptide is an effective anti-cancer cancer agent which can be used for treating cancer.

*Miscellaneous*

Although Miller et al. (WO 00/61597) is not presently considered prior art, it is still considered to be a reference of high relevance because it appears to disclose the claimed invention. For instance, please see (for example) claims 1, 7, 8-11, and 18-21.

*Conclusion*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



DAVE T. NGUYEN  
PRIMARY EXAMINER

J. Eric Angell  
May 15, 2003